II. Remarks

Reconsideration of the present application as amended is respectfully requested.

A. Status Of The Claims

Claims 1-20, 23-29, and 34 are pending in this application. Claims 1-20, 23-29 and 34 have been amended without prejudice. Claims 21 and 22 have been cancelled without prejudice. New claims 36 and 37 have been added. Support for new claims 36 and 37 can be found, e.g., in original claim 33, at page 8, lines 16-23 of the specification, and throughout the specification. It is respectfully submitted that no new matter has been added by virtue of this amendment.

B. Rejections under 35 U.S.C. § 112

Claim 25 was rejected under 35 U.S.C. 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically the Examiner states that "[c]laim 25 recites 'the respiratory disorder is COPD' which is vague and indefinite."

This rejected is traversed. The term "COPD" is a term known in the art as an abbreviation for "chronic obstructive pulmonary disease." This term can be found at page 3, lines 7-8 of the specification. Although this term is known in the art, the claim has been amended without prejudice to include the phrase "chronic obstructive pulmonary disease".

Claims 21-22 were also rejected under 35 U.S.C. 112, second paragraph, "as being indefinite in that it fails to point out what is included or excluded by the claim language". The Examiner states that "[t]his claim is an omnibus type claim."

In response claims 21-22 have been cancelled without prejudice.

In view of the aforementioned, the Examiner is respectfully requested to remove the 35 U.S.C 112 rejections over claims 25 and 21-22.

C. Rejections under 35 U.S.C. § 103

1. Claims 17-18 and 21-22 under 35 U.S.C. 103(a) over Britto (6,253,762) optionally in view of Carling et al. (5,674,860).

The Examiner states that "[i]t is deemed obvious to one of ordinary skill in the art at the time the invention was made to look at the guidance provided by Britto and utilize a composition containing fluticasone and formoterol. One would be motivated to do so since Britto teaches a preferred combination of actives is fluticasone and bronchodilators. Although, Britto does not exemplify formoterol, Britto states that formoterol is a bronchodilator and may be combined with fluticasone. Therefore one could reasonably expect success since the art teaches the functional equivalency of the instant bronchodilator and Britto's exemplified bronchodilator (salmeterol) and it is obvious to substitute one functionally equivalent compound with another functionally equivalent."

The Examiner further states that "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Britto and Carling et al and utilize fluticasone and [the] instant bronchodilator. One would be motivated to do so since Carling et al teach the instant bronchodilator has a longer duration of action to provide less nocturnal wăking than conventional bronchodilators. Further, Carling states that the instant bronchodilator acts rapidly to provide immediate relief. Therefore, one would be motivated to use formoterol due to the advantages taught by Carling." The Examiner further notes that "the step of administering the composition does not have patentable weight in a product claim."

This rejection is traversed. Britto is directed to "a metered dose inhaler having all or part of its internal surfaces coated with one or more fluorocarbon polymers, . . . for

dispensing an inhalation drug formation comprising fluticasone propionate . . .optionally in combination with one or more other pharmacologically active agents or one or more excipients." See Abstract. Further, at column 1, lines 63-67, Britto describes that "coating the interior can surfaces of MDI's with a fluorocarbon polymer significantly reduces or essentially eliminates the problem of adhesion or deposition of fluticasone propionate on the can walls and thus ensures consistent delivery of medication in aerosol from the MDI." (*emphasis added*).

Carling is directed to formoterol and/or a physiologically acceptable salt and/or solvate thereof and budesonide combinations for simultaneous, sequential or separate administration by inhalation in the treatment of an inflammatory respiratory disorder, such as asthma. See Abstract.

It is respectfully submitted that Britto fails in the very least to teach, hint or suggest a "dry powder inhaler" as recited in present claim 17. Britto also fails to teach, hint, or suggest the inhaler containing formoterol or pharmaceutically acceptable salt thereof and fluticasone or pharmaceutically acceptable salt thereof in "separate compositions" as recited in present claim 17.

Further, it is respectfully submitted that the combination of Carling et al. with Britto does not cure the deficiencies of Britto, as the combination of Britto and Carling fail to teach, hint, or suggest a dry powder inhaler containing formoterol or a pharmaceutically acceptable salt thereof, and fluticasone, or a pharmaceutically acceptable salt thereof in separate compositions as recited in present claim 17. (*emphasis added*).

Therefore, the Examiner is respectfully requested to remove this rejection.

2. Claims 1-10, 16-29, and 34 under 35 U.S.C. 103(a) over Palmer (5,270,305) in view of Carling et al. (5,674,860).

The Examiner states that "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Palmer and Carling et al and utilize fluticasone and [the] instant bronchodilator. One would be motivated to do so since Carling et al teach the instant bronchodilator has a longer duration of action to provide less nocturnal waking than conventional bronchodilators. Further, Carling et al. state that the instant bronchodilator acts rapidly to provide immediate relief. Therefore, one would be motivated to look to Carling et al and substitute Palmer's bronchodilator with formoterol due to the advantages taught by Carling et al. One would expect similar results since both references teach a steroid anti-inflammatory and a bronchodilator for respiratory disorders as asthma."

This rejection is traversed. It is respectfully submitted that one of ordinary skill in the art would not be motivated to substitute salmeterol (Palmer's bronchodilator) with formoterol (Carling's bronchodilator), as Palmer states "[W]e have found these two compounds [e.g., salmeterol and fluticasone,] to be particularly compatible and complementary in their activity and thus highly effective in the treatment of asthma and other respiratory disorders." See column 2, lines 21-24 (emphasis added). There is no indication in Palmer that fluticasone would be compatible with other β_2 agonists nor is their any indication in Carling et al. that formoterol would be compatible with other steroids. Therefore is respectfully submitted that one of ordinary skill in the art would not be motivated to combine the β_2 agonist of Carling et al. with the steroid of Palmer.

Further, it is respectfully submitted that the method of the present invention produces unexpected results over the combinations described in Palmer and Carling et al. Unexpectedly, as demonstrated in Example 1, a combination of formoterol/fluticasone has a greater change in band density (which is proportional to the increase in

glucocorticoid receptor translocation into the nucleus) than the combination of salmeterol/fluticasone or the combination of formoterol/budesonide.

To support this argument, the results in Example 1, Table 1 indicate that the combination of salmeterol/fluticasone has a percentage change in band density of **231 ± 26** and the combination of formoterol/budesonide has a percentage change in band density of **197 ± 10**. Unexpectedly, the combination of formoterol/fluticasone has a change in band density of **312 ± 26**.

Therefore, is respectfully submitted that the method of treating or alleviating a respiratory disorder comprising administering an effective amount of the active ingredients formoterol, or a pharmaceutically acceptable salt thereof, and fluticasone, or a pharmaceutically acceptable ester thereof as recited in claim 1 is not taught, hinted or suggested by Palmer and Carling.

Further, Palmer and Carling fail to teach, hint or suggest the at least 20% improvement in glucocorticoid receptor translocation into the nucleus by the administration of a therapeutically effective amount of formoterol and fluticasone as recited in claim 29.

The Examiner is therefore respectfully requested to remove this rejection.

3. Claims 11-15 under 35 U.S.C. 103(a) over Palmer (5,270,305) in view of Carling et al. (5,674,860) in further view of WO 97/47286.

The Examiner states that "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to combine Palmer, Carling et al, and WO [92/47286] and utilize the instant propellant. One would be motivated to do so since WO teaches the advantages that the instant propellant system provides. Therefore, one would be motivated to use HFA to provide a stable propellant system and a homogenous suspension of the drug and propellant. One would expect similar results since Palmer

also teaches the use of propellants when administering the composition via an aerosol system."

The arguments above with respect to Palmer and Carling are also applicable with respect to this rejection, and it is respectfully submitted that WO 97/47286 fails to cure the deficiencies of the combination of the Palmer and Carling et al references.

The Examiner is therefore respectfully requested to remove this rejection.

In view of the above, it is respectfully submitted that the 35 U.S.C. 103(a) rejections should be removed.

III. Conclusion

It is now believed that the above-referenced rejections have been obviated and it is respectfully requested that the rejections be withdrawn. It is believed that all claims are now in condition for allowance.

According to currently recommended Patent Office policy the Examiner is requested to contact the undersigned in the event that a telephonic interview will advance the prosecution of this application.

An early and favorable action is earnestly solicited.

Respectfully submitted,

DAVIDSON, DAVIDSON & KAPPEL, LLC

By: _____

Robert J. Paradiso
Reg. No. 41,240

Davidson, Davidson & Kappel, LLC
485 Seventh Avenue, 14th Floor
New York, New York 10018
(212) 736-1940